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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/513,888	02/25/2000	Carlo M. Croce	9855-30U1	6972

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EXAMINER
LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/513,888	CROCE ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24 and 100-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23 and 24* is/are allowed.

6)☒ Claim(s) *100-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/16/02 has been entered.

Receipt is also acknowledged of a supplemental response, filed 6/17/03 as Paper No. 29. The arguments presented in Paper No. 29 have been fully considered. Any rejection of record in the previous office action, mailed 3/11/02 as Paper No. 19, not addressed herein is withdrawn. Claims 23-24, 100-144 are pending and under consideration in the instant application.

Sequence Compliance

Receipt is acknowledged of a substitute sequence listing, computer readable form (CRF) and statements from applicants' representative concerning the substitute listings (Paper No. 23, filed 9/16/02). The papers have been entered into the file and the case is now in sequence compliance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 118-121, 141-142 and 144 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for reasons of record in Paper No. 19, mailed 3/11/02.**

Response to Arguments

Applicant's arguments filed in Papers No. 22 & 29 (filed 9/16/02 and 6/17/03, respectively) have been fully considered but they are not persuasive. The responses essentially argue: 1) the examiner's rejection is really based on what the examiner perceives as an underlying lack of operability or utility due to the alleged lack of success of gene therapy, 2) the examiner's rejection does not address an alleged absence of information in the specification which would allow a person of ordinary skill in the art to make and use the claimed invention, 3) it is improper to base an enablement rejection under 35 USC 112 1st on grounds of lack of utility unless there is an appropriate basis for making the rejection under 35 USC 101, 4) none of the references cited by the examiner teach that "gene therapy" is totally incapable of achieving a useful result, 5) the fact that an animal cell may be used in a method for gene therapy does not, even under the examiner's analysis, make it a non-enabled subject matter, 5) additional uses for the claimed cells are known and discussed in the specification, 6) the ordinary skilled artisan would be able to make the recited pharmaceutical compositions and/or transfect animal cells in order to arrive at the claimed invention, 7) techniques for the preparation, identification and insertion of such molecules into eukaryotic cells was well known in the art at the time of filing, 8) the examiner only used 4 of the 8 Wands factors in making the rejection, 9) a consideration of

the Wands factors does not provide an analytical framework for determinations of enablement, but only for analysis of whether the experimentation required to practice the claimed invention is undue, 10) the examiner has not met the burden of showing that any experimentation is undue because it does not consider the evidence of enablement as a whole and is based upon an apparent prejudice against "gene therapy", 11) the examiner generalizes but does not provide technical or legal support to support her generalizations, 12) based upon the references cited by the examiner, applicants assume the examiner takes the term to mean insertion of the claimed polynucleotide into a host genome and subsequent expression of such polynucleotides, 13) the examiner concedes the skill level of the art is high, 14) the high level of skill in the art favors applicants as greater quantity/complexity of experimentation is considered routine in high skill disciplines, 15) the examiner improperly applies Wands by stating that the art of the invention is unpredictable, 16) the art encompassed by the claimed invention is predictable, 17) the enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claims, 18) information that is routine in the art need not be included in the disclosure, 19) at least for some of the claims, the assertion that they are "broad" is inaccurate, 20) successful gene therapy data was available at the time of filing (3 references were cited), 21) it is incorrect to rely only on predictability in determining enablement.

With regard to assertions concerning the number of Wands factors considered in making the rejection, the examiner clearly stated that all of the Wands factors were considered in making the rejection (Paper No. 19, page7, 2nd full paragraph in section 12). With regards to assertions that the rejection is merely a 101 utility rejection in disguise, this assertion is inaccurate and

unsupportable. The examiner made a full-blown Wands analysis of the instant claims in view of all of the Wands factors and reached the conclusion that the claimed invention is not enabled. The fact that the claims read on gene therapy applications was only one factor in this Wands analysis. The fact that the success of gene therapy is unpredictable at this stage in the development of the field *is* an important factor when considered as part of the whole analysis. This fact means that whatever amount of research that must be done in order to make and use the claimed invention will be unpredictable, greatly influencing the determination of whether the research required is undue. Allegations that the examiner is simply biased against gene therapy methods are inaccurate and unsupportable. The rejection was made not only in terms of the field being complex and unpredictable, but also in light of the lack of significant teachings concerning the correlation of FEZ1 function and any particular type of cancer.

References cited in the response of Paper No. 38 might indicate that some types of gene therapy have achieved some degree of success, but there is no clear indication the references would have made practicing the claimed invention any more predictable at the time of filing. For example, the references themselves do not appear to be of record in the file and it is difficult to judge the degree of "success" in each instance. Nor is it possible to judge whether the references shed any light on which cancers might be specifically correlated with FEZ1 activity. Finally, it is noted that two of the references are post-filing date publications.

Assertions that the high level of skill in the art favors applicant as greater quantities and complexity of experimentation is considered routine in high skill disciplines is unsupported by any reference or legal finding. Even if one were to concede that the level work required to practice the claimed invention is routine, which is in no way conceded here, the experimentation

required would still be deemed undue due to the amount of unpredictable experimentation that would be required in order to reduce the invention to practice.

The assertion that the specification teaches other uses for the claimed cells is unsupported by any direction by applicants to any part of the specification to support the assertion. As the examiner stated in making the rejection, the only disclosed use for the claimed cells is as part of a "gene therapy" method.

Claims 100-143 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in Paper No. 19, mailed 3/11/02.**

Response to Arguments

Applicant's arguments filed in Papers No. 22 & 29 (filed 9/16/02 and 6/17/03, respectively) have been fully considered but they are not persuasive. The responses essentially argue: 1) the original application as filed contained the full sequence of the human FEZ1 gene (SEQ ID NO: 1), 2) each of the claim polynucleotides (which are portions of or homologous to SEQ ID NO: 1 containing the recited residues) were disclosed at least as part of SEQ ID NO: 1, 3) the initially disclosed sequence included all of the 'sub' sequences identified in the priority application, as well as others that have not been claimed, 4) the applicants have disclosed a broad range of polynucleotides and the specific ones claimed are not new matter, 5) the applicants can

think of no clearer way to indicate "possession" of the invention than to provide the primary nucleotide sequence, 6) the written description requirement under 112 1st paragraph is satisfied when a primary sequence of a polynucleotide is provided, 7) the point that individual sub-sequences aren't pointed out in the specification is irrelevant, and 8) there is no functional criticality to the endpoints.

The nucleotide sequence described by SEQ ID NO: 1 is over 9000 base pairs in length. Given that applicants are reciting limitations for "portions" of SEQ ID NO: 1 that are variable in length, the number of different subsets of SEQ ID NO: 1 to choose from is nearly incalculable (e.g. every possible 20 nucleotide fragment over the entire 9 kb, plus every 21 nucleotide fragment available over the entire 9 kb, plus every 22 nucleotide fragment over the entire 9 kb, etc.). Thus, the assertion that it is not NEW MATTER to arbitrarily choose specific fragments from the extraordinarily broad genus of such fragments embraced by the rejected claims when the entire primary sequence is disclosed is inaccurate and unsupportable.

The assertion that there is no functional criticality to the endpoints is disingenuous at best. This appears to be an argument that all of the possible fragments of SEQ ID NO: 1 are functional equivalents to one another. If this is true, then it stands to reason that the fragments taught by, for example, Chader et al, make obvious all of the other possible fragments found within SEQ ID NO: 1. Applicants are attempting to have it both ways by claiming, on the one hand, that their invention is unique and novel of the prior art by arbitrarily choosing portions of SEQ ID NO: 1 to carve around the prior art while simultaneously claiming, on the other hand, there is nothing functionally important concerning the particular recited portions of SEQ ID NO: 1. Applicants have thus far failed to indicate where support can be found in the instant

application for the specifically recited portions of SEQ ID NO: 1 in the rejected claims. Therefore, the claims remain rejected on the basis of the introduction of impermissible NEW MATTER into the claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 120-121, 142 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. **This is a new rejection.**

Each of the claims is directed to a cell comprising an isolated polynucleotide of the invention. The instant specification teaches that at least one intended use for the claimed polynucleotides is human gene therapy. As such, the claims can be read as to encompass a cell within a human, or the human subject itself. Therefore, the claims are directed to non-statutory subject matter. It would be remedial to amend the claims to read "an isolated animal cell" in order to distinguish the recited cell from cells in a human animal.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr., PhD
Examiner
Art Unit 1636

Ggl